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## Supporting Information

### Sugar-Based Gemini Surfactant with a Vesicle-to-Micelle Transition at Acidic pH and a Reversible Vesicle Flocculation Near Neutral pH

Markus Johnsson, Anno Wagenaar, and Jan B. F. N. Engberts

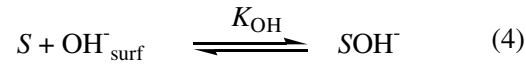
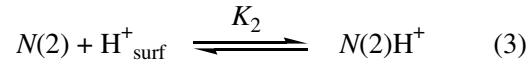
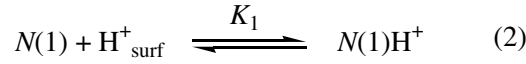
**Poisson-Boltzmann Model.** The PB cell model was used to calculate the surface potential of the vesicles for a given surface charge density. Only a short description of how it was adapted will be given here since the details of the model are described in the literature.<sup>1</sup> To describe the general electrostatic effect we have solved the Poisson-Boltzmann equation in the spherical symmetry<sup>2</sup>

$$\frac{1}{r^2} \frac{d}{dr} \left( r^2 \frac{d\phi}{dr} \right) = \frac{-F}{\epsilon_0 \epsilon_r} c_0 (\exp(-e\phi/k_B T) - \exp(e\phi/k_B T)), \quad (1)$$

$$R < r \leq b$$

assuming that only monovalent ions are present in the solution (15 mM buffer or 15 mM NaCl). In eq 1,  $\phi$  is the electrostatic potential,  $F$  is the Faraday constant,  $\epsilon_0 \epsilon_r$  is the permittivity of water,  $r$  is the radial distance from the center of the vesicle,  $k_B T$  is the Boltzmann temperature,  $e$  is the elementary charge,  $R$  is the vesicle radius (80 nm) and  $c_0$  is the salt concentration at the cell boundary ( $b$ ) (where  $\phi(b) = 0$ ). The boundary conditions specifying a solution to eq 1 are  $d\phi/dr|_b = 0$  and  $d\phi/dr|_R = -\sigma/\epsilon_0 \epsilon_r$ , where  $\sigma$  is the surface charge density.

We assume that there are three equilibrium reactions at the vesicle surface that determine the vesicle surface charge density, i.e. binding of two protons and one OH<sup>-</sup> according to



where  $N(1)$ ,  $N(2)$  and  $S$  are the respective binding sites on the surfactant head group (or at the vesicle surface) and  $K_1$ ,  $K_2$  and  $K_{OH}$  are the equilibrium constants associated with each binding site. The degree of binding ( $f$ ) to the respective binding site is given by

$$f_{N(i)} = \frac{K_i [H^+]_{\text{bulk}} \exp\left(\frac{-e\phi_s}{k_B T}\right)}{1 + K_i [H^+]_{\text{bulk}} \exp\left(\frac{-e\phi_s}{k_B T}\right)}; i = 1, 2 \quad (5)$$

$$f_s = \frac{K_{OH} [OH^-]_{\text{bulk}} \exp\left(\frac{e\phi_s}{k_B T}\right)}{1 + K_{OH} [OH^-]_{\text{bulk}} \exp\left(\frac{e\phi_s}{k_B T}\right)} \quad (6)$$

where  $\phi_s$  is the surface potential. From the degree of occupancy we calculate the surface charge density according to

$$\sigma = \frac{e}{a_{surf}} (f_{N(1)} + f_{N(2)} - f_s) \quad (7)$$

where  $a_{surf}$  is the surfactant head group area. Note that we have here assumed that the binding site area of both protons and hydroxide ions is the same ( $110 \text{ \AA}^2$ ). Using a fixed set of binding constants, we adjust the pH (assumed to be equal to  $-\log[H^+]_{bulk}$ ) until the surface charge density in eq 7 is the same as the surface charge density used in the solution of eq 1. The binding constants were varied until the best fit to the experimental data was obtained. Note that the calculated potential is the surface potential ( $\phi_s$ ) which is not exactly the same as the  $\zeta$ -potential since the latter is determined at some small (unknown) distance out from the vesicle surface (at the shear plane).<sup>3</sup> Nevertheless, the satisfactory agreement between experiment and calculation shows that the model appears to describe the system rather well.

### Synthesis.

**General.** All reactions were carried out in distilled anhydrous solvents under a nitrogen atmosphere using oven-dried glassware. Melting points (uncorrected) were determined using a Koffler melting point microscope.  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra were run on a Varian Gemini 200 or a Varian VXR 300 spectrometer. Elemental analysis was carried out by Mr. J. Hommes in the Analytical Department of the University of Groningen. D(+)-glucose was purchased from Merck, Oleyl alcohol and 1,8-diamino-3,6-dioxaoctane were obtained from Fluka and  $\text{NaBH}_3\text{CN}$  and 10% Pd/C were from Acros.

**Bis(1-amino-1-deoxy-D-glucityl)3,6-dioxaoctane.** This bolaamphiphile was prepared as previously described<sup>4</sup> by catalytic hydrogenation of D-glucose (in 5% excess) and 1,8-diamino-3,6-dioxaoctane in the presence of 10% palladium on carbon. The product was purified by recrystallization to yield white crystals, mp  $136\text{--}138^\circ\text{C}$ .  $^1\text{H}$ -NMR (300 MHz,  $\text{D}_2\text{O}$ ):  $\delta = 2.55\text{--}2.73$  (m, 8H),  $3.52\text{--}3.82$  (m, 20H).  $^{13}\text{C}$ -NMR (50.3 MHz,  $\text{D}_2\text{O}$  ( $\text{CH}_3\text{OH}$  ref.)):  $\delta = 48.15, 57.02, 63.49, 70.04, 70.12, 71.38, 71.60, 71.71, 71.77$ .

**Bis(N-octadecene-9-yl-1-amino-1-deoxy-D-glucityl)3,6-dioxaoctane (1, HCl salt).** To a well-stirred suspension of 0.524 g (1.1 mmol) of the bolaamphiphile in 25 mL of methanol at room temperature was added 0.1 g (1.6 mmol) of  $\text{NaBH}_3\text{CN}$  and 0.611 g (2.3 mmol) of oleyl aldehyde.<sup>5,6</sup> After 15 min a few drops of concentrated acetic acid were added to give a pH of 6. This was repeated after 1 h (total added amount of acetic acid was 0.11 g). After stirring for 24 h the reaction mixture was a clear colorless solution. The solvent was evaporated under vacuum and in order to quench the excess of  $\text{NaBH}_3\text{CN}$  the reaction mixture was treated with 25 mL 2% HCl(aq) and stirred for 3 h. 50 mL of THF was added to the very viscous solution and the mixture was stirred for 10 min after which 9 g of NaCl(s) was added. The organic layer was separated and the aqueous layer was washed three times with 20 mL THF. The combined THF-layers were washed once with a saturated NaCl solution and the organic solvent was removed under vacuum. The residue was dissolved in 10 mL of distilled water and freeze-dried. Traces of NaCl were removed by dissolving the product in methanol and filtering the solution (3 times). Yield 1.13 g (97%).  $^1\text{H}$ -NMR (300 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta = 0.90$  (t, 6H),  $1.30$  (br s,

54H), 1.78 (br s, 4H), 2.04 (m, 8H), 3.2-3.95 (m, 30H), 4.18 (m, 2H), 5.35 (m, 4H).  $^{13}\text{C}$ -NMR (50.3 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  = 14.49, 23.75, 24.60, 27.73, 28.16, 30.36, 30.46, 30.62, 30.84, 33.07, 33.66, 54.65, 55.93, 57.17, 64.68, 65.87, 68.67, 71.44, 72.18, 130.74 (*cis*), 130.87 (*cis*), 131.41 (*trans*), 131.52 (*trans*). Anal. Calcd for  $\text{C}_{54}\text{H}_{108}\text{N}_2\text{O}_{12}\cdot 2\text{HCl}$ : C 61.75; H 10.56; N 2.67. Found: C 61.89; H 10.71; N 2.64.

**Bis(N-octadecene-9-yl-1-amino-1-deoxy-D-glucityl)3,6-dioxaoctane (1, neutral).** The HCl salt of **1** (see above) was stirred in a suspension of dry potassium carbonate in THF. Filtration and evaporation of the solvent gave the neutral gemini **1**.

## References and Notes

1. Gunnarsson, G.; Jönsson, B.; Wennerström, H. *J. Phys. Chem.* **1980**, *84*, 3114.
2. The solution to eq 1 was obtained using the computer program PBCell (Jönsson, B.; PBCell is a freeware program that can be downloaded at <http://www.memfound.lth.se/chemeng1/prog.html>).
3. An even better fit to the  $\zeta$ -potential data can be obtained by equating  $\zeta = \phi_\delta$ , where  $\phi_\delta$  is the electrostatic potential at a distance  $\delta$  from the vesicle surface. A commonly used value for  $\delta$  is 2 Å (Frens, G.; Overbeek, J. TH. G. *J. Colloid Interface Sci.* **1972**, *38*, 376; Eisenberg, M.; Gresalfi, T.; Riccio, T.; McLaughlin, S. *Biochemistry* **1979**, *18*, 5213) which, if applied using the given set of binding constants, would give a better fit to the data, in particular at higher potentials. However, since we do not know the exact magnitude of  $\delta$  in the present system, we have chosen to present the surface potential ( $\phi_s$ ) instead of  $\phi_\delta$  in Figure 4 of the paper.
4. Pestman, J. M.; Terpstra, K. R.; Stuart, M. C. A.; van Doren, H. A.; Brisson, A.; Kellogg, R. M.; Engberts, J. B. F. N. *Langmuir* **1997**, *13*, 6857.
5. Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.
6. The oleyl aldehyde was prepared from oleyl alcohol as described in ref. 5. The *cis/trans* ratio of the oleyl alcohol was 75/25 as determined by  $^1\text{H}$ -NMR. No isomerisation was observed during the synthesis. Assuming that the reaction of the oleyl aldehyde with the bola amphiphile occurs without any preference for either the *cis* or the *trans* form, we can calculate that the final product should have the following chain distribution: (*cis*, *cis*) = 9/16, (*cis*, *trans*) = 6/16 and (*trans*, *trans*) = 1/16.